R E M A R K S

Claim Amendments and New Claims

The amendment to claim 8 regarding the terminology of "matrix-type ... the drug is dispersed uniformly in the particles" is supported in the specification on page 7, lines 13 to 16.

Claim 18 is newly added. The terminology in claim 18 of "submerged drying method" is supported by the description on page 8, lines 5 to 7 of the specification.

Claim 19 is newly added. The terminology in claim 19 of "betamethasone" and "polylactic acid having a weight-average molecular weight of 20,000" is supported by Example 1, Process for producing drug-containing fine particles, on page 10 of the specification.

Presently Claimed Invention

The presently claimed invention is directed to a method of treating a disease of a posterior segment of an eye comprising

administering subconjunctivally to a patient an effective amount for treatment of an injection comprising fine particles containing a drug and enabling the drug concentration in a retina-choroid to be sustained, the disease of the posterior segment of the eye being uvetis, cytomegalovirus retinitis, age-related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy or retinal detachment, the fine particles containing the drug being a matrix-type, wherein the drug is dispersed uniformly in the fine particles, and a particle diameter of fine particles being 50 nm to 150 μm.

Anticipation Rejections Under 35 USC 102

Claims 8, 10 and 12 were rejected under 35 USC 102 as being anticipated by Peyman (USP 6,395,294) for the reasons set forth on pages 3 to 4 of the Office Action.

As discussed hereinabove, applicants' claim 8 was amended hereinabove to further define the type of fine particles in an injection to "a matrix-type, wherein the drug is dispersed uniformly in the fine particles." This amendment serves to

clarify the differences between the presently claimed invention and Peyman.

In drug-containing fine particles, various types are known, such as a matrix-type and a capsule-type (see page 7, lines 13 to 17 of the present specification). However, Peyman does not teach which type of drug-containing fine particles is preferable for the treatment of posterior segment disease.

Further, applicants' new claim 18 is directed to a drug-containing fine particles being produced by a submerged drying method. In contrast thereto, Peyman does not describe or suggest how to manufacture a drug-containing fine particles for the treatment of a posterior segment disease.

In view of the above, withdrawal of the 35 USC 102 rejection based on Peyman is respectively requested.

Although claims 8, 10 and 12 were not rejected under 35 USC 103, it is respectfully submitted that the presently claimed invention is not obvious in view of Peyman for the following reasons.

Peyman teaches a subconjunctival injection solution comprising a drug-containing fine particles as a vitreous delineating agent. However, Peyman primarily relates to a surgical method to alleviate a structural disorder.

Further, Peyman does not teach or suggest how to deliver a drug to the posterior segment of the eye and enable the drug concentration in a retina-choroid to be sustained by subconjunctival administration. Consequently, it is respectfully submitted that Peyman would not lead one of ordinary skill in the art to the presently claimed invention.

In contrast to Peyman, in the presently claimed invention, drug-containing fine particles of a matrix-type are employed, wherein the drug is dispersed uniformly in the fine particles (see Example 1 of the present specification). The present inventors discovered after intense studies that the subconjunctival administration of such fine particles enables the drug concentration in the retina-choroid to be sustained (see Table 1 on page 13 of the present specification, which is reproduced hereinbelow).

Table 1: Betamethasone concentrations in retina-choroids (μg/g tissue)

	Control group (suspension)	Microsphere injection
Two days after administration	0.54±0.35	0.70±0.26
Seven days after	0.96±0.54	0.18
14 days after	≦ Detection limit	0.17±0.06
21 days after	≦ Detection limit	0.10±0.02
28 days after	≦ Detection limit	0.09±0.02

It is respectfully submitted that the above Table 1 provides a showing of unexpected results, especially since Peyman does not teach or suggest which type of drug-containing fine particles are preferable to enable a drug concentration in the retina-choroid to be sustained.

Claims 8, 10 and 12 were rejected under 35 USC 102 as being anticipated by Wong et al. (USP 5,869,079) for the reasons set forth on pages 5 to 6 of the Office Action.

Wong et al. teach implants which can be implanted at various sites, including the suprachoroid, the subconjunctiva, and the like. further, Wong et al. also teach that their implants introduced into the suprachoroid can deliver drugs to the choroid and the retina. Furthermore, it was pointed out in the Office Action that Wong et al. teach the use of the implants for medical and veterinary uses.

However, applicants disagree with the reasons for this rejection based on the following. Although Wong et al. teach that their implants can be implanted at the subconjunctiva, Wong et al. do not describe or suggest that their implants introduced into subconjunctiva can deliver drugs to the choroid and the retina. In contrast thereto, drugs in the presently claimed invention are delivered to the retina-choroid, and the drug concentration therein is sustained by administering an injection comprising a drug-containing fine particles subconjunctivally to

a patient, thereby treating a posterior segment disease. Consequently, the presently claimed invention is clearly different from Wong et al. Moreover, Wong et al. do not specifically disclose which disease can be treated by their implants, while in the presently claimed invention, the target disease is a posterior segment disease, including uvetis, cytomegalovirus retinitis, proliferative vitreoretinopathy, retinal detachment, age-related macular degeneration or diabetic retinopathy.

It is therefore respectfully submitted that applicants' present claims are novel over Wong et al.

Although applicants' claims 8, 10 and 12 were not rejected under 35 USC 103, the presently claimed invention is not obvious in view of Wong et al. for the following reasons.

Wong et al. teach that their implants are introduced into suprachoroid and deliver drugs to the choroid and the retina. However, injection into the suprachoroidal space is likely to be a burden on patients, since the choroid is located at the backside of the eye. On the other hand, although subconjunctival

injection hardly causes disorders of ophthalmic tissues and a burden on patients is minimal (see page 2, lines 7 to 3 from the bottom of the present specification), it has been difficult to sustain the concentration of drugs (see page 3, lines 5 to 8 from the bottom of the present specification). Thus, the present inventors conducted intense studies to develop a sustained drug delivery system to the posterior segment of the eye by subconjunctival injection (see page 3, lines 18 to 21 of the present specification). Consequently, the presently claimed invention and Wong et al. are clearly different in the problem to be solved. Therefore, it is respectfully submitted that Wong et al. would not lead a person of ordinary skill in the art to the presently claimed invention.

Further, in Wong et al., it is easily expected that drugs administered at the suprachoroid can be delivered to the retina-choroid, since the choroid is adjacent to the retina. In contrast thereto, in the presently claimed invention, it is unpredictable that a subconjunctival administration of a drug-containing fine particles enables drug concentration in the retina-choroid to be sustained (see Table 1 of the present specification, which is set

forth hereinabove), since the conjunctiva and the retina-choroid are anatomically remote tissues.

Claims 8, 10 and 12 were rejected under 35 USC 102 as being anticipated by Bowman et al. (USP 6,378,526) for the reasons set forth on pages 3 to 4 of the Office Action.

Bowman et al. teach a method for treating a posterior segment disease, such as a macular degeneration by inserting a cannula through a location on an exterior surface of the sclera over the posterior segment of the eye. Consequently, Bowman et al. do not describe or suggest a method for treating a posterior segment disease by administering an injection subconjunctivally.

Although Bowman et al. teach that their cannula can be inserted into the sclera through conjunctiva, it is emphasized that the cannula merely penetrates the conjunctiva to administer a drug to the sclera (see column 7, lines 7 to 29 of Bowman et al.). Thus, the presently claimed invention is clearly different from Bowman regarding the administration site.

Therefore, it is respectfully submitted that applicants' present claims are novel over Bowman et al.

Although claims 8, 10 and 12 were not rejected under 35 USC 103, it is respectfully submitted that the presently claimed invention is not obvious in view of Bowman et al. for the following reasons.

The administration site (i.e., sclera over the posterior segment of the eye) in Bowman et al. is relatively near the target tissue (i.e., retina-choroid). Therefore, it is readily expected that drugs administered at the sclera over the posterior segment of the eye can be delivered to the retina-choroid. Further, Bowman et al. teach that the sclera is vascular and the material injected therein is not removed or cleared from the eye (see column 4, lines 39 to 50 of Bowman et al.).

In contrast to Bowman et al., in the presently claimed invention, the administration site (i.e., subconjunctiva) is remote from the target tissue (i.e., retina-choroid) and the conjunctiva is a vasculated tissue. Because of these disadvantages, it has been considered difficult to deliver drugs injected subconjunctivally to the posterior segment and sustain drug concentration therein. However, the present inventors discovered that a subconjunctival administration of drug-

containing fine particles enable drug concentration in the retina-choroid to be sustained (see Table 1 of the present specification, which is set forth hereinabove). Consequently, this is an unpredictable result.

Withdrawal of each of the 35 USC 102 rejections is therefore respectfully solicited.

Reconsideration is requested. Allowance is solicited.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

Respectfully submitted,

RICHARD S. BARTH
REG. NO. 28,180

FRISHAUF, HOLTZ, GOODMAN & CHICK, P.C.
220 FIFTH AVENUE, 16th FLOOR
NEW YORK, NEW YORK 10001-7708
Tel. Nos. (212) 319-4900
(212) 319-4551/Ext. 219
Fax No. (212) 319-5101
E-Mail Address: BARTH@FHGC-LAW.COM
RSB/ddf

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